

File No. PG4860USw

REMARKS

Currently claims 1-10 and 16 are pending in the application.

The present application relates to a pharmaceutical composition comprising (2S)-2-amino-4-[[2-(ethanimidoylamino)ethyl]thio]butanoic acid, a pharmaceutically acceptable bulking agent and one or more antioxidants or chelating agents.

Claims 9-10 have been rejected under 35 USC §112. It is the Examiner's position that the application is not enabled for prevention or "prophylaxis". Applicant has amended claim 9 thereby making this rejection of it moot. New claim 17 is directed to prophylaxis of specified indications set forth on page 6, lines 4-6, of the specification. Therefore, it is respectfully requested that the Examiner reconsider this rejection and withdraw it.

Claims 1, 8-10, and 16 have been rejected under 35 USC §102(b) as being anticipated by WO93/13055. It is the Examiner's position that the reference generically discloses (2S)-2-amino-4-[[2-(ethanimidoylamino)ethyl]thio]butanoic acid. Further, the Examiner suggests that the reference utilizes (i) a bulking agent containing small amounts of cellulose and starch and as well as (ii) an antioxidant to treat humans with a condition where there is an advantage of inhibiting NO production from L-arginine by the action of NO synthase.

WO 93/13055 discloses a structure which generically covers Applicant's claimed compound, (2S)-2-amino-4-[[2-(ethanimidoylamino)ethyl]thio]butanoic acid (pages 3-7). Applicant's particular claimed compound is nowhere specifically described or named. The reference provides a list of acids suitable for forming salts. This list includes, *inter alia*, phosphoric acid (page 8). However, the list is a generic disclosure, as there is nothing singling out the phosphoric acid from other named acids. Applicant's claimed combination is, likewise, not described in the reference. Additionally, there is no teaching in WO 93/13055 to use antioxidant, and/or chelating agents, such as Applicant's claimed antioxidant or chelating agents in solid pharmaceutical compositions. Therefore, Applicant's claimed invention is not identically disclosed in this reference. Accordingly, WO 93/13055 does not anticipate the invention set

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forth in the instant claims. Therefore, it is requested that this rejection of the claims be reconsidered and withdrawn.

The invention of claims 1-10, and 16 have been rejected under 35 USC 103(a) as being *prima facie* obvious in view of WO 93/13055 in combination with WO 98/30537 and US Patent No. 6,297,281. It is the Examiner's contention that WO 93/13055 teaches a pharmaceutical composition, bulking agent, and antioxidant for a human condition where there is an advantage of inhibiting NO production such as in arthritis. It is further pointed out by the Examiner that WO 93/13055 does not specifically teach solvates or chelating agents (and amounts thereof). The Examiner cites WO 98/30537 as teaching "salts and solvates thereof." Further, the Examiner states that this reference does not recite the particular solvates, mono- and tri- hydrates, but asserts that one of ordinary skill in the art would appreciate the presence of such hydrates from the mention of solvates in the reference. The Examiner argues that US Patent No. 6,297,281 teaches a pharmaceutical composition containing at least one NO synthase inhibiting substance, at least one oxygen reactive form trapping substance such as a substance with antioxidant properties, in particular ascorbic acid.

According to the Examiner, the motivation to combine the three references is as follows. Since WO 98/30537 cites WO 93/13055, these two references are, therefore, combinable. And US Patent No 6,297,281 can be combined with WO 98/30537 and WO 93/13055 because '281 teaches the combination of at least one NO synthase inhibitor combined with another agent having antioxidant properties; both WO references teach NO synthase inhibitors, and WO 93/13055 teaches the combination of a NO synthase inhibitor combined with an antioxidant as well.

Applicant's invention is not obvious in view of the disclosure of the three references cited by the Examiner. There is no teaching or suggestion in any of the references to arrive at Applicant's combination as claimed. Nothing in the three references cited by the Examiner suggests Applicant's particular claimed combination, Applicant's specific compound, nor the desirability of combining said compound with a bulking agent and an antioxidant or chelating agent. The Examiner has impermissibly used the teaching in Applicant's application to

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hunt for and attempt to find Applicant's claimed elements among the myriad of teachings of the three references.

WO 93/13055 does not mention Applicant's specific compound ((2S)-2-amino-4-([2-(ethanimidoylamino)ethyl]thio) butanoic acid); nor does it mention antioxidant or chelating agents for solid pharmaceutical compositions. Likewise, WO 98/30537 does not mention Applicant's particular compound in combination with antioxidant or chelating agents in solid pharmaceutical compositions. It does however contemplate "a salt, solvate, or physiological functional derivative" of the compounds embodied in its generic structure. US Patent No. 6,297,281 concerns a pharmaceutical composition containing at least one NO synthase inhibiting substance and at least one oxygen reactive from trapping substance, optionally with a pharmaceutically acceptable support. It too is silent regarding a specific compound or the specific combination claimed by Applicant. There is nothing in these three references that points to or suggests Applicant's specifically claimed combination. It is only from having first seen Applicant's invention as embodied by Applicant's claims that the Examiner is led to cite and combine the references in the present impermissible manner. Accordingly, it is requested that this rejection be reconsidered and withdrawn for the reasons set forth above.

Applicant has made U.S. Patent Nos. 5,889,056 and 6,156,341 of record in an Information Disclosure Statement filed concurrently with this response.

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The Commissioner is hereby authorized to charge any fees required or credit any overpayment to Deposit Account No. 07-1392.

Respectfully submitted,

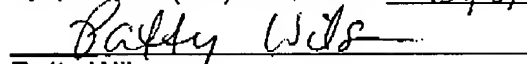


Bonnie L. Deppenbrock
Attorney for Applicant
Registration No. 28,209

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GlaxoSmithKline
Corporate Intellectual Property
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709-3398
Phone: 919-483-1577
Facsimile: 919-483-7988

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Patty Wilson